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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,951	10/13/2000	Jeffrey L. Cleland	GEN02-002-US	8871

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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/687,951	CLELAND ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,22,23,25-29,31,33,34,36 and 40-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20;22,23,25-29,31,34 and 40-43* is/are rejected.

7)☒ Claim(s) *33 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/3/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 20, 22-23, 25-29, 31, 33-34, 36 and 40-43 are pending.

Applicants' amendment filed on December 13, 2006 is acknowledged. Applicants' response has been fully considered. Claims 20 and 22 have been amended, and claim 30 has been cancelled. Thus, claims 20, 22-23, 25-29, 31, 33-34, 36 and 40-43 are examined.

Withdrawn Claim Objections

2. The previous objection of claims 30 is withdrawn in view of applicants' cancellation of the claim in the amendment filed December 13, 2006.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 20, 22, 23, 25-29, 31, 34 and 40-43 are rejected under 35 U.S.C 103(a) as being unpatentable over Suzuki *et al.* (US Patent 6,197,326, filed October 14, 1998) in view of Igari *et al.* (US Patent 5,416,071, published on May 16, 1995).

Suzuki *et al.* teach an intra-articular preparation for the treatment of arthropathy, which comprises microcapsules of a biocompatible, high molecular weight substance such as PLGA, homopolymer or copolymer of lactic acid, glycolic acid, caprolactone and others (column 1, lines 45-60; column 2, line 66-column 3, line 30; claims 25-27), and a drug such as steroid agents, cyclosporin (a cyclic peptide; column 3, lines 44-64; claims 28); and the microcapsules can be

administered in the form of injection by suspending it in a dispersion medium, where injection-grade water may be used as the dispersion medium, further, a buffer, an isotonicity (e.g., NaCl; claim 23), and others can be added, particularly a microcapsule-dispersing medium which contains hyaluronic acid, or chondroitin sulfate or salts thereof is particularly preferred (column 4, line 60-column 5, line 8; claims 34). Suzuki *et al.* also teach injection of beclomethason propionate in a dose of 1 mg (the drug content is 8.8-10.2 % in microcapsules corresponding to microcapsules in 11.4-9.8 mg for Examples 1-5, Table 1; Test 1) or dexamethasone in a dose of 9 mg (the drug content is 3.8 % in microcapsules corresponding to microcapsules in 237 mg for Example 8, Table 2; Test 4) into knee joint of rabbits. Although the reference does not specifically indicate the volume used in the injection, it does indicate the use of 10 ml in the test of release of dexamethasone-containing microcapsule samples, thus the concentration of microcapsules can be 1 or 24 mg/ml in the injection (Test 3; claim 31). However, Suzuki *et al.* do not teach the concentration of hyaluronic acid in the formulation.

Igari *et al.* teach a pharmaceutical composition suitable of injection comprising erythropoietin (Examples 1-11) or other biological agents such as NGF (Example 12) and hyaluronic acid, where hyaluronic acid, a high molecular weight compound which is known to be biodegradable and pharmacologically injectable at the concentration of 0.01 to 3% (weight to volume), more preferably about 0.05 to 2% (column 3, lines 63-column 4, line 21; column 7, lines 51-58; column 13, lines 43-46).

At the time of invention was made, it would have been obvious that one of ordinary skill in the art has been motivated to combine the two references to administer a biologically active agent by injecting a formulation comprising hyaluronic acid, buffer and a microcapsule of a

biocompatible polymeric substance and a biologically active agent as taught by Suzuki *et al.* using the concentration of hyaluronic acid as taught by Igari *et al.* (claims 20, 22, 29, 40-43) because hyaluronic acid at the concentration of 0.01 to 3% (weight to volume) would allow the formulation be easily administered using a small-gauge needle such as 26 G (column 3, lines 63-column 4, line 11), which results in the claimed invention and was, as a whole, *prima facie* obvious at the time the claimed invention was made.

Response to Arguments

Applicants indicate claims 20 and 22 as newly amended herein now recite the phrase "wherein the concentration of the polymeric matrix is about 1 mg/mL to about 500 mg/mL of formulation. Neither Suzuki, or Igari, taken alone or together, teach or suggest a polymeric concentration of 1 mg/mL to about 500 mg/mL as now recited in claims 20 and 22. The Office explicitly acknowledges this fact in its objection to, but not rejection of, claims 30, 31, 33 and 36. Thus, because Suzuki and Igari fail to render obvious independent claims 20 and 22 as amended, the documents fail to render obvious claims 23, 25-29, 34 and 40-43 dependent therefrom. Therefore, the rejection should be withdrawn (pages 7-8 of the response).

Applicants' response has been fully considered, however, the arguments are not fully persuasive because Suzuki *et al.* teach injection of beclomethason propionate (Test 1) in a dose of 1 mg (the drug content is 8.8-10.2 % in microcapsules, corresponding to microcapsules in 11.4-9.8 mg for Examples 1-5, Table 1) or dexamethasone in a dose of 9 mg (the drug content is 3.8 % in microcapsules, corresponding to microcapsules in 237 mg of Example 8, Table 2; Test 4) into knee joint of rabbits. Although the reference does not specifically indicate the volume used in the injection, it does indicate the use of 10 ml in the test of release of dexamethasone-

containing microcapsule samples, thus the concentration of microcapsules in the injection can be 1 or 24 mg/ml (Test 3), which meets the limitation for the concentration of polymeric matrix in the claimed invention, thus, the rejection is maintained.

Claim Objections

4. Claims 33 and 36 are objected to as being dependent upon a rejected base claim.

Conclusion

5. Claims 20, 22, 23, 25-29, 31, 34 and 40-43 are rejected, and claims 33 and 36 are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PRIMARY EXAMINER

CMK
February 26, 2007